REMARKS

Reconsideration of the above-identified patent application in view of the amendment above and the remarks below is respectfully requested.

Claims 9 and 12 have been canceled in this paper. Claims 1, 3-5, 7, 10 and 13-14 have been amended in this paper. New claims 15 and 16 have been added in this paper. Therefore, claims 1-8, 10-11 and 13-16 are pending and are under active consideration.

At the outset of the outstanding Office Action, the Patent Office makes the following suggestions:

> The Examiner recommends that the following changes be made to the claims to place the application in better condition for allowance: in claim 1, all instances of "and/or minor ischemic myocardial damage namely" be replaced with "involving" & all instances of "and ischemic membrane destruction" be deleted. Claims 3, 4, 5 & 7 should be amended similarly as claim 1.
>
> Claim 9 & 12 should be cancelled (see discussion of claim 9 below) and claims 13 & 14 should be rewritten in independent form.

Applicants have adopted all of the above recommendations of the Patent Office to place the claims in better condition for allowance.

The outstanding Office Action also includes the following comments regarding the specification:

> The attempt to incorporate subject matter into this application by reference to prior publications mentioned in the specification is improper because these references should be submitted in a proper Information Disclosure Statement in order to be fully considered. Proper correction is required.

The foregoing comments made by the Patent Office are not fully understood by Applicants. In particular, Applicants do not understand to which "prior publications mentioned in the

specification" the Patent Office's comments are directed. In any event, Applicants are submitting herewith an Information Disclosure Statement in which copies of all of the documents referenced in the present specification are submitted for consideration by the Patent Office. In addition, Applicants note that Applicants previously filed an Information Disclosure Statement on November 13, 2003, in which all of the documents referenced in the Amendment of September 22, 2003 were submitted for consideration by the Patent Office. (Although the Patent Office makes reference in the outstanding Office Action to receipt of the November 13, 2003 Information Disclosure Statement, an annotated copy of the listing of citations submitted by Applicants was not enclosed with the outstanding Office Action.[1]) If the Patent Office requires anything else in addition to the foregoing Information Disclosure Statements, Applicants respectfully request that the undersigned be contacted, preferably by telephone.

Claims 1-14 stand rejected under 35 U.S.C. 112, first paragraph, "because the specification, while being enabling for recognizing and diagnosing acute myocardial infarction, does not reasonably provide enablement for all acute coronary syndromes." In support of the rejection, the Patent Office states the following:

> The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with the claims.

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[1] On the Office Action Summary page of the outstanding Office Action, the Patent Office indicates that "Information Disclosure Statement(s) (PTO-1449) Page No(s) 9" is attached to the subject Office Action. However, Applicants did not receive said attachment with the outstanding Office Action. Accordingly, Applicants respectfully request that, in its next correspondence, the Patent Office clarify the status of the November 13, 2003 Information Disclosure Statement and, in addition, enclose a copy of the annotated form.

> Upon inspection of the instant specification, it appears that all correlations are directed towards CCTD and myocardial infarction. While applicant does point out that levels of CCTD below the limit may be indicative of other coronary troubles, such a correlation does not appear to be absolute, as is the case with myocardial infarctions. In fact, it appears that more of a correlation is made between such coronary troubles as angina pectoris and troponin levels. At best, on page 22, the specification does seem to support instable angina pectoris along with myocardial infarction which may be diagnosed on choline measurements. The instant claims, however, are directed to CCTD measurement and content and do not consider troponin levels. Thus, the instant claims do not seem to be commensurate in scope with instant disclosure. Further clarification and/or correction is required.

Later in the Office Action, the Patent Office continues as follows:

> Applicant's arguments filed 11/17 have been fully considered but they are not persuasive. Applicant has argued that the specification is enabled. However much of the specification is speculative as to the relationship between CCTD and various forms of angina. There are some instances where in some forms of angina there is no CCTD elevation. Further clarification is required.

Insofar as the foregoing rejection pertains to claims 9 and 12, Applicants respectfully submit that the foregoing rejection is moot in view of Applicants' cancellation herein of claims 9 and 12. Insofar as the foregoing rejection pertains to claims 1-8, 10-11 and 13-14, Applicants respectfully traverse the foregoing rejection.

As best understood by Applicants, the Patent Office is apparently acknowledging in the outstanding Office Action that the present specification is enabling (i) for recognizing and diagnosing acute myocardial infarctions based on CCTD levels and (ii) for recognizing and diagnosing unstable angina pectoris based on choline levels[2]. At the same time, however, the Patent

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[2] See the Patent Office's statement in the subject rejection that "the specification does seem to support instable angina pectoris along with myocardial infarction which may be diagnosed based on choline measurements."

Office is apparently contending that the specification is not enabling for recognizing and diagnosing unstable angina pectoris based on CCTD levels other than choline levels and for recognizing and diagnosing acute coronary syndromes other than acute myocardial infarction and severe forms of unstable angina pectoris. For at least the reasons given below, Applicants respectfully submit that the Patent Office has failed to establish a *prima facie* case of non-enablement with respect to recognizing and diagnosing unstable angina pectoris based on CCTD levels other than choline levels.[3]

At the outset, Applicants note that, as explained in MPEP 2164.04 and 2164.07, it is **not** Applicants' responsibility to prove enablement. Instead, the specification is presumed to be enabling, and it is the Patent Office's burden to prove non-enablement. To prove non-enablement, the Patent Office must provide a reasoned basis for a person of ordinary skill in the art who has read the specification to doubt the objective truth of the statements contained in the specification. Given that the present specification clearly states, at more than one location in the specification, that CCTD levels may be used to recognize and diagnose unstable angina pectoris, it is the burden of the Patent Office to prove that a person of ordinary skill in the art who has read the specification would be within reason to question the objective truth of the statement that CCTD levels may be used to recognize and diagnose unstable angina pectoris. Applicants respectfully submit that the Patent Office has failed to meet its burden in showing a reasoned basis for doubting the objective truth of the statement in the specification that CCTD levels can be used to recognize and diagnose unstable

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[3] Applicants note that the claims have been amended so that acute coronary syndromes other than acute myocardial infarction and severe forms of unstable angina pectoris are no longer recited. Therefore, to the extent that the present rejection relates to such acute coronary syndromes, the rejection is moot.

angina pectoris. In particular, the Patent Office has not provided any factual or scientific basis upon which one of ordinary skill in the art would reasonably question the operability of the invention. In fact, the only explanation given by the Patent Office as to why the specification is allegedly non-enabling is that "more of a correlation is made between such coronary troubles as angina pectoris and troponin levels" and that the correlation between CCTD and unstable angina pectoris "does not appear to be absolute" and "is speculative" as "[t]here are some instances where in some forms of angina there is no CCTD elevation."

In reply, Applicants note that the Patent Office has not provided any predicate for its conclusions, either by specific reference to statements in the present specification or by reference to other documents. For example, the Patent Office has provided no explanation or support for its conclusion that the correlation between CCTD and unstable angina pectoris is speculative. Similarly, the Patent Office has not identified in which instances there was no CCTD elevation for severe forms of unstable angina pectoris. In any event, apart from the fact that the Patent Office has not provided a factual or scientific predicate for concluding that there is no correlation between CCTD levels and severe forms of unstable angina pectoris, Applicants respectfully submit that a proper reading of the present specification does, in fact, support Applicants' position that CCTD levels may be used to recognize and diagnose unstable angina pectoris.

For example, Applicants refer to the following passage bridging pages 19 and 20 of the present specification:

> As is well known, the prognosis of patients suffering from instable angina pectoris is worse if increased values of cardial troponins are discovered in the progress thereof (Ohmann, E.M. 1996, N Engl J Med 335:1333-41). It is assumed that these patients not only go through myocardial ischemia but also suffer myocardial

> micronecroses so that it cannot be excluded that, in future, these patients will be classified under microinfarctions when the AMI may be judged according to new classifications. It is essential that these patients be identified quickly because, as rule, they should be treated without delay and must undergo emergency angiography, if necessary. The examinations by the applicants have revealed that patients with angina pectoris and an uncomplicated course of the disease do not have elevated levels of CCTD, whereas the CCTD values are higher for all those patients with myocardial micronecroses. It follows from the results gathered thus far that all patients with acute coronary syndroms who are CCTD positive develop higher troponin values in the course of events. For patients with micronecroses, the serial examinations likewise showed that the results for CCTD were positive several hours sooner than for troponin I or troponin T. Moreover, it must be assumed that the method will be helpful also in diagnosing severe myocardial ischemias, e.g. upon catheter interventions in the coronaries or in case of diseases with an involvement of the myocardium, such as myocardites. The results obtained by the applicants prove that the method is precious both with the acute myocardial infarction and also with instable angina pectoris, in other words quite generally when there is suspicion of an acute coronary syndrom.

The foregoing passage does not support the Patent Office's apparent position that the specification does not show a correlation between severe forms of unstable angina pectoris and elevated CCTD levels. Instead, what the foregoing passage indicates is that, for patients with angina pectoris and an uncomplicated course of the disease (in other words, patients that do **not** suffer from a severe form of unstable angina pectoris), elevated levels of CCTD were not observed, whereas, for patients with myocardial micronecroses (in other words, certain patients suffering from a **severe form of unstable** angina pectoris), elevated CCTD values were observed. The mere fact that the foregoing passage also indicates that, with respect to those patients in which elevated CCTD were observed (in other words, patients suffering from acute myocardial infarction or unstable angina pectoris), an increase in troponin levels was **also** observed, does not mean that troponin levels are

correlated with severe forms of unstable angina pectoris whereas CCTD levels are not.[4] Instead, the passage merely points out that the increase in CCTD levels was observable **sooner** than the increase in troponin levels and did not depend upon a measurement of troponin levels.

Moreover, Applicants have provided the Patent Office with additional evidence, establishing a correlation between increased CCTD levels and severe forms of unstable angina pectoris. For example, in Danne et al., "Prognostic Implications of Elevated Whole Blood Choline Levels in Acute Coronary Syndromes," Am J Cardiol 91:1060-7 (2003), and in Wu et al., "Ischemia-Modified Albumin, Free Fatty Acids, Whole Blood Choline, B-Type Natriuretic Peptide, Glycogen Phosphorylase BB, and Cardiac Troponin," Caridac Markers, Second Edition, edited by Alan H.B. Wu, Human Press, Totowa, NJ (2003), copies of which were submitted in the Information Disclosure Statement of November 13, 2003, ample evidence is given of the strong correlation between elevated choline levels and high-risk unstable angina pectoris. The Patent Office has provided no contrary evidence regarding the usefulness of choline levels nor has the Patent Office provided any evidence to suggest that the results for CCTD levels generally would be different from those for choline levels. As noted above, it is the Patent Office's burden to show why the results for CCTD levels would not be expected to be consistent with those for choline levels, not Applicants' burden to prove the opposite.

In summary, the Patent Office has provided no reasonable basis for doubting that CCTD may be used as a marker for early recognition and diagnosis of severe forms of unstable angina pectoris. Therefore, the claims must be considered to be enabled by the present specification.

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[4] If anything, the fact that an increased level of troponins was also observed where an increased level of CCTD was observed actually buttresses Applicant's position that there is a correlation between an increase in CCTD levels and severe forms of unstable angina pectoris.

In any event, with respect to claim 13, Applicants note that claim 13 is limited to acute myocardial infarctions. In view of the fact that the Patent Office acknowledges in the outstanding Office Action that the present specification is "enabling for recognizing and diagnosing acute myocardial infarction," Applicants respectfully submit that there should be no question that claim 13 is fully enabled by the present specification. Therefore, the foregoing rejection of claim 13 should be withdrawn and claim 13 should immediately be allowed.

Similarly, with respect to new claim 15, since the Patent Office has indicated that the present specification is enabling for the recognition and diagnosis of severe forms of unstable angina pectoris using choline levels, claim 15 should immediately be allowed.

New claim 16 is allowable for at least the same reasons given above for claim 1.

Accordingly, for at least the above reasons, the foregoing rejection should be withdrawn.

Claim 9 stands rejected under 35 U.S.C. 112, second paragraph "as being incomplete for omitting essential structural cooperative relationships of elements, such omission amounting to a gap between the necessary structural connections. See MPEP §2172.01."

Applicants have canceled claim 9. Accordingly, the foregoing rejection is moot and should be withdrawn.

In conclusion, it is respectfully submitted that the present application is now in condition for allowance. Prompt and favorable action is earnestly solicited. If this paper does not place the application in condition for allowance, Applicants respectfully request that the Patent Office contact the undersigned by telephone so that attempts may be made to expedite prosecution of the application.

If there are any fees due in connection with the filing of this paper that are not accounted for, the Examiner is authorized to charge the fees to our Deposit Account No. 11-1755. If a fee is required for an extension of time under 37 C.F.R. 1.136 that is not accounted for already, such an extension of time is requested and the fee should also be charged to our Deposit Account.

Respectfully submitted,

Kriegsman & Kriegsman

By: _____

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Dated: April 2, 2004

I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to: Mail Stop Fee Amendment, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450 on April 2, 2004.

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Edward M. Kriegsman
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Dated: April 2, 2004